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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/639,690	08/16/2000	ANDREW K. BENSON	101997-5	3073

21125 7590 10/01/2002

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EXAMINER	
KATCHEVES, KONSTANTINA T	
ART UNIT	PAPER NUMBER
1636	16

DATE MAILED: 10/01/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No. 09/639,690	Applicant(s) BENSON, ANDREW K.
	Examiner Konstantina Katcheves	Art Unit 1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,9,14,17-21 and 23-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,9,14,17-21 and 23-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-6, 8, 9, 14, 17-21 and 23-31 are pending in the present application.

Response to Amendment

The rejection of Claims 14, 17-20 and 23-25 under 35 U.S.C. 102(e) as being anticipated by Heynecker (U.S. Patent 6,057,100) has been withdrawn in view of Applicant's Amendment filed 2 July 2002.

The rejection of Claims 14, 17-20 and 23-25 under 35 U.S.C. 103(a) as being unpatentable over Heyneker et al. in view of Anderson, Bruckner-Lea et al., Bergeron et al., Nakayama et al., and Tauxe have been withdrawn.

Claims 1-6, 8, 9, 14, 17-21 and 23-25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Heyneker et al., Anderson, Bruckner-Lea et al., Bergeron et al., Nakayama et al., and Tauxe, further in view of Megerle (U.S. Patent 5,874,046) for the reasons of record set forth in the prior Office Actions.

Claims 14, 17-20, and 23-25 stand rejected under 35 U.S.C. 102(e) as being anticipated by Balch (U.S. Patent 6,083,763) for the reasons of record set forth in the Office Action mailed 15 June 2001.

Claims 1-6, 8, 9, 14-21, and 23-25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Balch, as applied to claims 14, 17-20, and 23-25 above, in view of Megerle (U.S. Patent 5,874,046), and further in view of Anderson, Bruckner-Lea et al. (1999), Bergeron et al., Nakayama et al., and Tauxe (1997) for the reasons of record set forth in the Office Action mailed 15 June 2001.

Claims 1-6, 8, 9, 14, 17-21 and 23-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention

Response to Arguments

In response to the pending rejections Applicant has argued that Heynecker fails to meet all the limitations of the claimed invention because it fails to meet the step, which requires the correlation of the output distribution to "predictive qualitative properties." Applicant also argues that Balch et al. fail to teach this limitation and also fails to teach database mining. Balch et al. is provided in combination with several references including Tauxe under 35 U.S.C. 103. Tauxe et al. is provided for the teaching of a datab se, which is discussed more extensively below. Moreover, it is evident from the rejection under 35 U.S.C. 112, second paragraph, that "predictive qualitative properties" is a vague and indefinite term such that Applicant's arguments fail to obviate either Heynecker or Balch as prior art. Applicant argues against the references individually, however, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 and 14-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heyneker et al., as applied to claims 1-4, 14, and 17-19 above, and further in view of Anderson et al. (U.S. Patent 5, 922, 591), Bruckner-Lea et al. (1996), Bergeron et al. (U.S. Patent 6,001,564), Nakayama et al. (U.S. Patent 5795717), and Tauxe (1997).

Heyneker et al. teaches methods using oligonucleotide probe arrays to detect bacteria in food samples. Heyneker et al. does not teach automated fluidics.

Anderson et al. teaches a combination of oligonucleotide probe arrays and automated fluidics for use in nucleic acid based diagnostic applications and other applications (see Abstract and claims 52 and 53). Anderson et al. teach that following amplification and/or labeling, the nucleic acid sample is incubated with the oligonucleotide array in the hybridization chamber, and hybridization between the sample nucleic acid and the probes on the array are detected (column 15, lines 4-11). Anderson et al. teach that data gathering methods are known in the art and readily automated for detection and interpretation of data (column 16 lines 61-67 and column 17

lines 1-43). Anderson et al. teach that there are different chambers for carrying out different functions, such as a sample collection chamber, an extraction chamber, an amplification chamber and a hybridization chamber (see above and column 23; further details are given, for example, in column 38 and throughout the reference). Anderson et al. teach that the system of the invention can be used in methods for diagnosing the presence of infectious agents and that the analyses can be performed in parallel on a large number of individual samples (column 39). Anderson et al. does not specifically teach food product testing.

Bruckner-Lea et al. teach strategies for automated sample preparation, nucleic acid purification of nucleic acids in environmental and food processing samples. Bruckner-Lea et al. teach that their automated fluidic system provides nucleic acids in a form suitable for PCR or microarray-based detectors. (See page 63). The mesofluidic system is described on page 64, and state that the automated system is rapid and does not require a highly skilled technician (page 68). Bruckner-Lea et al. do not teach simultaneous detection of a plurality of species.

Bergeron et al. teach methods that use probes to rapidly detect and identify common bacterial pathogens. Specific probes for different bacterial pathogens are taught. Bergeron et al. teach that a pool of specific oligonucleotide probes is used to identify simultaneously more than one bacterial species (column 11, lines 64-67; column 13 lines 35-50). Bergeron et al. also teach that the method can be performed directly on samples obtained from food (see column 15, line 60, and claim 2). Bergeron et al. do not specifically teach probe arrays as a method of detection, and Bergeron et al. do not teach automated fluidics.

Nakayama et al. teach oligonucleotide primers complementary to sequences that encode genes related to pathogenicity, such as toxin genes, of pathogenic bacteria. Nakayama et al.

teach that these are used as probes for detection of pathogens in samples, e.g., clinical isolates and food specimens (see column 1 and columns 3-4). The primers are used to amplify DNA from the suspected bacterial species. Nakayama et al. teach detection by agarose gel electrophoresis in the specification (see the figures and column12), although the method of detection in the claims is left open. Nakayama et al. do not teach probe arrays, automated fluidics, or database mining.

Tauxe reviews foodborne diseases, including information about when contamination occurs in the production process (see page 428; such information relates to the "process history parameters" of instant claim 9). Tauxe also reviews surveillance strategies, which include electronic systems (see page 430). The data from the surveillance is used to monitor outbreaks and to trace large-scale trends in foodborne disease (page 430) and the data is also used to monitor foodborne parasitic and viral infections. Tauxe does not teach probe arrays or automated fluidics.

At the time of the invention of the instant application, one of ordinary skill in the art would have been motivated to detect a plurality of species in food products, since many microorganisms can contaminate food and cause disease. Since there are many different bacterial and other species that contaminate food, as reviewed by Tauxe, one would have been motivated to use a probe array that could detect more than one species simultaneously. Heyneker et al. teach probe arrays for detection of microorganisms in food samples and that a plurality of pools of probes can be put onto the array, and Bergeron et al. and Nakayama et al. teach specific probes for bacteria and teach that they can be used more than one bacterial species simultaneously. Bruckner-Lea teach the value of an automated fluidic system for preparing

DNA for detection from samples, such as food samples (such as rapidity of the process), and Anderson et al. teach an automated fluidic system for preparing DNA and detection by probe arrays. Additionally, since Tauxe teach the value of electronic surveillance measures with respect to food, the ordinary artisan would have been motivated to put information into an electronic (hence, computer-operated) database and to mine the database for relevant information. Thus, it would have been obvious to one of ordinary skill in the art to combine the teachings of these references to detect species in food using automated preparation and amplification of DNA and probe arrays and to use databases. Success would have been expected.

Claims 1-9 and 14-21 and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heyneker et al., Anderson, Bruckner-Lea et al., Bergeron et al., Nakayama et al., and Tauxe, as applied to claims 14-20 and 23-25 above, and further in view of Megerle (U.S. Patent 5,874,046).

Megerle teaches detection with an array of oligonucleotides of target microorganisms, and teaches that to offer independent confirmation of the detection of a target microorganism, a plurality of oligonucleotides may be synthesized that are complementary to different segments of the target microorganism's DNA (see column 9). Megerle also teaches output distributions that include the presence of an organism and its location; such distributions are linked to a network so that decisions could be made based on this information (see column 4).

At the time of the invention of the instant application, the ordinary artisan would have been motivated to combine the teachings of Megerle regarding the use of multiple probes to

different segments of a microorganism's DNA with the teachings of the other cited references regarding detection of microorganisms with probe arrays because Megerle teaches that this offers confirmation of the detection of a target microorganism, and thus would improve the confidence level in the data obtained. Success would have been expected.

Claims 14, 17-20, and 23-25 are rejected under 35 U.S.C. 102(e) as being anticipated by Balch (U.S. Patent 6,083,763).

Balch teaches multiplexed molecular analysis of samples with probe arrays. Balch teaches preparation of an array of probes from a plurality of different species (see for example column 38, lines63-67), sample preparation including extracting target molecules from the sample (see for example column 10 lines 54-58), PCR amplification if necessary (see for example column 35 lines 1-11), and hybridizing the DNA (after labeling) to the probe array. The samples for the method can be air, water, and food samples or patient samples for detection of multiple microorganisms and determination of a microbial spectrum of the amount and type of microorganisms, such as pathogenic microorganisms, present in the sample. See for example columns 33-37 and 38-39, Examples III and VII. The process can also be automated with fluidics (see column 5 , lines 51-67 to column 6, line43).

Claims 1-9, 14-21, and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Balch, as applied to claims 14, 17-20, and 23-25 above, in view of Megerle (U.S. Patent

5,874,046), and further in view of Anderson, Bruckner-Lea et al. (1999), Bergeron et al., Nakayama et al., and Tauxe (1997) (of record).

As noted above, Megerle teaches detection with an array of oligonucleotides of target microorganisms, and teaches that to offer independent confirmation of the detection of a target microorganism, a plurality of oligonucleotides may be synthesized that are complementary to different segments of the target microorganism's DNA (see column 9). Megerle also teaches output distributions that include the presence of an organism and its location (see above.

The teachings of Anderson, Bergeron et al., Nakayama et al., and Tauxe are described in the previous Office Action. Briefly:

Anderson et al. teach oligonucleotide probe arrays and automated fluidics for hybridization methods of nucleic acid based diagnostic and other applications. Anderson et al. teach data gathering methods.

Bruckner-Lea et al. teach methods involving automated fluidics in sample preparation, nucleic acid purification from environmental and food processing samples.

Bergeron et al., like Balch, also teach methods of detection of simultaneously more than one bacterial species with oligonucleotide probes. That is, multiple species analysis has been proposed before by several inventors.

Nakayama et al. teach oligonucleotide primers complementary to sequences encoding genes related to pathogenicity and also teach culturing.

Tauxe review foodborne diseases, including information systems to detect when and where contamination occurs in the production process. Tauxe also reviews electronic

surveillance strategies in which data is used to monitor outbreaks and trace trends in foodborne disease; that is, Tauxe teaches databasing information and mining databases.

At the time of the invention of the instant application, the ordinary artisan would have been motivated to detect a plurality of species in food products and in other samples, since many microorganisms can contaminate food (or other samples) and cause disease. One would have been motivated to use a probe array as taught by Balch to obtain an output distribution of the types and number of microorganisms present or any other data determinable by the multiplex methods of Balch, to use automated methods to save time and effort as taught by Balch and Anderson, to detect multiple sequences for each species as taught by Megerle to confirm detection data, to use genes involved in pathogenicity for probe detection as taught by Nakayama, and to store the information in a database (as opposed to throwing it away or writing it down laboriously with pencil and paper) for easy retrieval and referral later, and for comparing against other databased information for such purposes as identifying a point in food preparation process at which contamination is occurring (as in the HACCP process reviewed by Tauxe) or for such purposes as contributing to and mining the information in electronic surveillance networks such as FoodNet (reviewed by Tauxe) to monitor outbreaks, infections, and other public health information. Success would have been expected.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 8, 9, 14, 17-21 and 23-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant recites the terms "food product," "foodstuff" and "food sample" in claim 1, for example. First, it is unclear what Applicant intends any of these terms to encompass. Are they interchangeable, or are they distinct limitations? Additionally, do any or all of these terms include all types of consumable foods, are they foods for human consumption, are they meat products, vegetable, processed foods, raw foods cooked foods? The terminology used would be considered vague and indefinite by one of skill in the art.

Applicant's claims also recite the term "output distribution." It is not clear what Applicant intends this term to mean. Applicant raises the question of what the output consists of and further how is it distributed. This phrase indicates that Applicant's method results in some sort of product, yet it is not clear what kind of product an "output distribution" really is.

Applicant's claims also recite the term "mining." This phrase without precise definition is unclear. Is "mining" a comparative process, a detection process, a discovery process or a physical process? This term requires precise definition in the specification in order to render the claims more precise. Morespecifically, what does Applicant intend database mining to mean?

The claims also recite the phrase, "predictive qualitative properties." Without a definitions or guidance from the specification, one of skill in the art would not be apprised of the metes and bounds of the present claims. This language is inherently qualitative thus rendering the claims unclear. Moreover, what are these properties, how are they measured, what are they predictive of and how are they predictive?

Applicant also recites limitations drawn to "food quality" and "processing conditions." Applicant has not defined what food quality or processing conditions are or how they are measured. There are no parameters or standards present by which to measure either food quality or processing conditions. Applicant also states that the target species could be correlated to "extrinsic parameters" that would be predictive of "food quality" and "processing conditions." However, there is no indication what these parameters are nor how are they measured. Moreover, in claim 17 Applicant recites "food safety" as wells as quality the same issues discussed above are raised by this term. Also, does Applicant intend that this limitation is similar to food quality or processing because safety is a limitation, which is not evident in the prior independent claims?

Applicant in claim 26 recites various qualitative properties, however, it is unclear how these properties relate to the output distribution or any prediction of food quality or processing conditions. Also, smell, texture and taste are all qualities that require a very subjective analysis and applicant has provided no quantitative or objective means to determine these qualities.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Konstantina Katcheves whose telephone number is (703) 305-1999. The examiner can normally be reached on Monday through Friday 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3388.

Konstantina Katcheves
October 1, 2002

DAVID GUZO
PRIMARY EXAMINER
David Guzo